REMARKS

A check for the fee for a three-month extension of time accompanies this response. Any fees that may be due in connection with filing this paper or with this application during its entire pendency may be charged to Deposit Account No. **06-1050**. If a Petition for extension of time is required, this paper is to be considered such Petition, and any fee charged to Deposit Account No. **06-1050**.

Claims 50-52 and 73-128 are pending in this application. Claims 89, 91, 94 and 99 have been amended to correct a typographical error. Claims 114-128 have been added. Basis for the added claims is found throughout the specification as originally filed. No new matter is added.

A DECLARATION under 37 C.F.R. §1.132 of Dr. Steven Fabijanski accompanies this response and is referred to as Fabijanski Declaration 4, in accordance with the designations adopted by the Examiner.

CORRECTION OF FIRST DECLARATION UNDER 37 C.F.R. §1.132 OF STEVEN FABIJANSKI (FABIJANSKI DECLARATION 1)

As a preliminary matter, Applicant wishes to note the correction of an inadvertent error in the first Declaration under 37 C.F.R. §1.132 of Dr. Steven Fabijanski (Fabijanski Declaration 1) that was submitted along with the response (dated July 16, 2003) to the first office action (mailed January 16, 2003). The error is in the designation of a cell line referred to in Fabijanski Declaration 1. Specifically, in that declaration (see p. 2 of Fabijanski Declaration 1), the cells containing a satellite artificial chromosome from which microcells were prepared was pAgII/B19-18, not the EC3/7C5 cell line referred to in the declaration. The pAgII/B19-18 cell line is, however, correctly described in Fabijanski Declaration 1 as a murine cell line containing a satellite artificial chromosome. The satellite artificial chromosome was generated by transfecting mouse LMtk$^-$ cells with DNA encoding a selectable marker (puromycin-resistance) and mouse rDNA. Elements from vector pAgIIa (described in Fabijanski Declarations 2 and 3 and the accompanying Declaration of Fabijanski) were subsequently incorporated

into the satellite artificial chromosome. Microcells were prepared from the B19-18 cells containing the resulting satellite artificial chromosome and fused with tobacco BY-2 protoplasts as described in Fabijanski Declaration 1. The accompanying Declaration of Steven Fabijanski (Fabijanski Declaration 4) also addresses this inadvertent error.

THE REJECTION OF CLAIMS 50-52 AND 73-113 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 50-52 and 73-113 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention for the reasons of record. Specifically, the Office Action maintains previous rejections based on an allegation that the term "satellite artificial chromosome" is unclear and questions "What is a satellite artificial chromosome?".

In traversing this rejection, Applicant's prior Responses to this allegation referred to many passages throughout the instant application that describe and characterize satellite artificial chromosomes in great detail. In the Office Action, it is now alleged that the citation to p. 94, lines 3-21, in support of the description of a satellite artificial chromosome as containing more heterochromatin than euchromatin is unpersuasive because the mouse megachromosome work is based on a number of assumptions, and relevance of this system to plants and plant SATACs is not apparent since Applicant has not described plant megachromosomes.

It is further alleged in the Office Action that the issue of how an artificial chromosome differs from a SATAC remains. Specifically, it is alleged on page 5 of the Office Action that in the absence of a clear distinction of how much more heterochromatin than euchromatin (such as, for example, "50%, 10%, 1% or will 1 nucleotide suffice?") is contained in a SATAC, the term remains undefined by the specification.

Applicant's assertion in the previous Response that the term "SATAC" is presumptively definite since it is recited in an issued claim (U.S. Patent No. 6,077,697) is also deemed unpersuasive in the Office Action. Two reasons are cited in the Office Action for this conclusion: (1) the instant claims are alleged to be effectively drawn to plant functional SATACs, which are not claimed in the patent except for claim 27 of the patent and (2) the Office Action was reviewed and signed by the Group Director of Technology Center 1600.

The rejection of the claims under 35 U.S.C. §112, second paragraph, is respectfully traversed.

RELEVANT LAW

Claims are not read in a vacuum but instead are considered in light of the specification and the general understanding of the skilled artisan. *Rosemount Inc. v. Beckman Instruments, Inc.,* 727 F.2d 1540, 1547, 221 USPQ 1, 7 (Fed. Cir. 1984), *Caterpillar Tractor Co. v. Berco, S.P.A.,* 714 F.2d 1110, 1116, 219 USPQ 185, 188 (Fed. Cir. 1983). When one skilled in the art would understand all of the language in the claims when read in light of the specification, a claim is not indefinite.

There are no requirements for terms to be defined in the claims when one of skill in the art can readily determine the meaning of the term based on the description and definitions provided in the specification. In this respect, an applicant is entitled to be its own lexicographer [see, *e.g.*, MPEP 2111.01 "Applicant may be his or her own lexicographer as long as the meaning assigned to the term is not repugnant to the term's well known usage and utilize terms within the claims that are clear from a reading of the specification. In re Hill, 73 USPQ 482 (CCPA 1947)."]. When applicant has provided definitions in the specification, the claims are interpreted in light of such definition.

THE CLAIMS

Claims 50-52 and 73-128 are pending. Claim 92 is directed to a method for producing a transgenic plant that includes introducing a satellite artificial

chromosome into a plant cell and growing the plant cell under conditions to produce a transgenic plant. All of the remaining claims are dependent on claim 92. The dependent claims specify particular types of plant cells or protoplasts, that the satellite artificial chromosome is a plant satellite artificial chromosome, and/or comprises heterologous DNA that encodes a gene product, and/or particular methods for the introduction of the satellite artificial chromosomes into plant protoplasts.

ANALYSIS

The Claim Term "Satellite Artificial Chromosome" is Clear Based on Descriptions and Definitions in the Application and the Use of Language Readily Understood by the Skilled Artisan

In reviewing the course of examination of the instant application, it is noted that the first instance in which the question of "what is a satellite artificial chromosome" was posed in rejecting the claims under 35 U.S.C. §112, second paragraph, was in the Office Action mailed October 22, 2003. This same question was repeated in each of the two subsequent office actions issued since that time. As a result, this Response represents the third communication to the United States Patent and Trademark Office in which the Applicant has addressed this question in connection with rebutting the alleged lack of clarity of the term "satellite artificial chromosome." The Applicant's repeated responses have been consistent in setting out how the application describes satellite artificial chromosomes as artificial chromosomes containing duplicated segments of DNA, which typically includes highly repetitive DNA, such as, for example, pericentric heterochromatic DNA and satellite DNA, that have more heterochromatin than euchromatin. In order to emphasize the more than adequate compliance of the claims with 35 U.S.C. §112, second paragraph, the Applicant, in each response, has cited numerous passages in the specification describing detailed analyses of all the aspects of this artificial chromosome referred to as a satellite artificial chromosome. These individual citations to

specific aspects of satellite artificial chromosomes (e.g., chromosomal functioning, staining patterns, DNA content, etc.) combine into the whole of the application and contribute to the overall characterization of satellite artificial chromosomes as artificial chromosomes containing duplicated segments of DNA, which typically includes highly repetitive DNA, and having more heterochromatin than euchromatin. The many citations to the application are abundant evidence that, in keeping with applicable law (as previously cited by the Applicant), the claims are not indefinite since one skilled in the art would understand all of the language in the claims when read in light of the specification (*see, e.g., Rosemount Inc. v. Beckman Instruments, Inc.,* 727 F.2d 1540, 1547, 221 USPQ 1, 7 (Fed. Cir. 1984), *Caterpillar Tractor Co. v. Berco, S.P.A.,* 714 F.2d 1110, 1116, 219 USPQ 185, 188 (Fed. Cir. 1983)).

It appears, however, that each of the different citations to the application has instead served as a new focal point on which Applicant's responses have been deemed "unpersuasive" in the office actions (including the instant Office Action). Such points include the following: (1) the alleged insufficiency of a recitation of the "properties" without providing the "essential elements" of a satellite artificial chromosome, (2) an alleged insufficiency of the teaching of the structural information of a chromosome by lack of a recitation of "the linear order" and "relationship" of a centromere, telomeres, an origin of replication and heterochromatin and (3) an alleged requirement of an explanation of the difference between a "functional stable chromosome" and a "fully functional stable chromosome." It is respectfully submitted that the continued piecemeal rejection of the claims under 35 U.S.C. §112, second paragraph, is thus based on the reading of excised pieces of the specification in isolation and without regard to the skilled artisan's understanding of standard terminology in the art, and therefore is improper.

Applicant maintains that the meaning of the term "satellite artificial chromosome" as embodied in the specification (and repeatedly restated in the

responses) is unequivocal and transcends the several specific points raised in the office actions so as to render them immaterial and discursive in a consideration of the definiteness of the claims. Applicant urges that based on the extensive teaching of the application **as a whole** and the general understanding of the skilled artisan, the claims readily satisfy the requirements of 35 U.S.C. §112, second paragraph. The application is filled with the details of many separate analyses of satellite artificial chromosomes that, considered as a whole, demonstrate that satellite artificial chromosomes are an artificial type of a macromolecule known in the art as a chromosome.

A Satellite Artificial Chromosome is a Type of Chromosome - the word "Chromosome" is a Clear and Definite Term of Art

As noted above, it is stated in several of the office actions that a "recitation of properties of a satellite artificial chromosome" (e.g., satellite DNA, nearly fully heterochromatic) does not: (1) "teach what the essential elements are," (2) "provide structural information" (e.g., the linear order of centromeres and telomeres, etc.) and (3) "address a fully functional chromosome." The office actions point to these alleged insufficiencies as the reason Applicant purportedly has not satisfactorily addressed the repeated question of "what is a satellite artificial chromosome." Applicant urges, however, that the alleged insufficiencies are **unrelated** to that question. Rather, these points in actuality concern a very different question, namely: "*what is a chromosome?*". It is respectfully submitted that this question cannot form the basis of a proper rejection of claims under 35 U.S.C. §112, second paragraph, as being indefinite; the term "chromosome" is a clear and definite term of art. As such, the skilled artisan is fully aware of what the term "chromosome" entails.

As is clear from the instant application, a satellite artificial chromosome is a type of **chromosome**. Applicant has extensively studied the satellite artificial chromosome type of artificial chromosome and provides the details and results

of these analyses in the instant application. The results confirm that the satellite artificial chromosome is indeed a type of macromolecule referred to in the art as a "chromosome" by criteria known to the skilled artisan as characterizing a chromosome. Thus, as set forth in the application and noted in previous responses to rejections of the claims under 35 U.S.C. §112, second paragraph, a satellite artificial chromosome is a chromosome, and as a chromosome, irrespective of its unique and distinctive properties, it: (1) is DNA and (2) carries out chromosomal functions such as, for example, (a) replication and segregation within cells for continued stable maintenance in a cell and its progeny and (b) carrying genes and providing the template for the expression of a gene. A significant portion of the application is dedicated to the details of studies demonstrating that a satellite artificial chromosome is in fact an artificial type of a basic macromolecule well-known in the art: **a chromosome**. The Applicant in the application thus strives to describe the discovery as much as possible in terms readily understood by the skilled artisan.

The skilled artisan possesses a knowledge of chromosomes and the basic structural components and functional features thereof sufficient to understand and recognize this nucleic acid-based composition that forms the basis of the specialized type of chromosomes described in the application and recited in the claims. Thus, the word "chromosome" which is part of the larger term "satellite artificial chromosome" includes within it the elements and functions known to the skilled artisan as being characteristic of this particular DNA-based composition. Accordingly, it is not necessary to explicitly recite the "essential elements," "linear order of structures" or "function" of a chromosome when using the term in a claim. By way of analogy, the skilled artisan also possesses a knowledge of cells such that the term "cell" is clear and definite when used in a claim without having to recite the "essential elements" (e.g., cytoplasm, membrane, nucleic acids, etc.) that make up a cell. As a term of art understood by the skilled artisan, the term "chromosome" is definite and clear such that it

comports with the requirements of 35 U.S.C. §112, second paragraph, when used in a claim. As evidence of the clarity of the term "chromosome," a search for the term in claims of patents issued since 1976 using the U.S. Patent Office database resulted in 1087 patents.

The Application Describes a Satellite Artificial Chromosome as an Artificial Chromosome Containing Duplicated Segments of DNA (Including Highly Repetitive DNA) and having More Heterochromatin than Euchromatin

Applicant has repeatedly and consistently responded to the question of "what is a satellite artificial chromosome" raised in rejections of the claims under 35 U.S.C. §112, second paragraph, by referring to the extensive description in the application of these compositions as artificial chromosomes having more heterochromatin than euchromatin and duplicated DNA segments that typically includes highly repetitive DNA, such as, for example, pericentric heterochromatic DNA and satellite DNA. The distinctive characteristics of the satellite artificial chromosomes as painstakingly characterized in the application make them readily identifiable and distinguishable by the skilled artisan. Therefore, as urged in the previous responses to the rejections, in light of the whole application, the term "satellite artificial chromosome" is clear and definite.

Nonetheless, it is alleged in the Office Action that in the absence of a clear distinction of how much more heterochromatin than euchromatin (such as, for example, "50%, 10%, 1% or will 1 nucleotide suffice?") is contained in a satellite artificial chromosome, the term remains undefined. Applicant respectfully submits, however, that the term is clear based on the definitions and characteristics provided in the application. Not only does the application describe the differences between heterochromatin and euchromatin and how to distinguish and determine the relative amounts of each of these types of chromatin in a chromosome, the skilled artisan likewise possesses a knowledge of heterochromatin and euchromatin sufficient to recognize when a chromosome

contains more heterochromatin than euchromatin. For example, on p. 17, line 28, through page 18, line 5, of the application, euchromatin and heterochromatin are referred to as having their "recognized meanings." Specifically, euchromatin refers to chromatin that stains diffusely and that typically contains genes, and heterochromatin refers to chromatin that remains unusually condensed and that has been thought to be transcriptionally inactive. Furthermore, highly repetitive DNA, *e.g.*, satellite DNA, is typically located in heterochromatin, particularly pericentric heterochromatin. Methods for visualizing and comparing the relative amounts of heterochromatin and euchromatin are also known in the art and referred to in the application. For example, C-banding and fluorescence *in situ* hybridization (FISH) using labeled nucleic acid probes (*e.g.*, satellite DNA probes) can be used to visualize heterochromatin and highly repetitive DNA. The extent of heterochromatin determined in such a manner can be compared to the total content of a chromosome and/or to the extent of euchromatin determined by techniques similarly known to the skilled artisan. Accordingly, the skilled artisan can readily determine if a chromosome contains more heterochromatin than euchromatin. Thus, as taught in the instant application, a discernable excess of heterochromatin as compared to euchromatin in an artificial chromosome is a clear distinction defining the term "satellite artificial chromosome" that is readily understood by the skilled artisan. Assigning a specific numerical value to the excess of heterochromatin over euchromatin is unnecessary for purposes of defining a satellite artificial chromosome.

The Question as to Whether Applicant has Described a Plant Satellite Artificial Chromosome Does Not Form Proper Grounds for Rejecting the Claims under 35 U.S.C. §112, Second Paragraph

It is further alleged in the Office Action that the description of a satellite artificial chromosome provided in the application as being an artificial chromosome containing more heterochromatin than euchromatin is not

persuasive evidence of the definiteness of the term because the mouse megachromosome work is based on a number of assumptions, and relevance of this system to plants and plant SATACs is not apparent since Applicant has not described plant megachromosomes. It is respectfully submitted that this line of reasoning does not constitute an appropriate basis for rejection of the claims under 35 U.S.C. §112, second paragraph.

First, it is noted that the pending claims are directed to a method for producing a transgenic plant. The method includes introducing a satellite artificial chromosome into a plant cell. New dependent claim 114 specifies that the satellite artificial chromosome is a plant satellite artificial chromosome.

Second, the standard for satisfying the definiteness requirement under 35 U.S.C. §112, second paragraph, is straightforward: a claim is definite if one skilled in the art would understand all of the language in the claim when read in light of the specification. If a claim meets this standard, the number and particular types of satellite artificial chromosomes specifically exemplified in the application have no impact on the *definiteness* of the claim. As set forth by Applicant herein and throughout examination of the application, the term "satellite artificial chromosome" is clear and definite in accordance with the applicable standards; therefore, any rejection of the claims based on an allegation of indefiniteness of this term is not valid. The instant application provides elaborate descriptions of analyses of an exemplary satellite artificial chromosome (*i.e.*, a mouse megachromosome) that was generated in a mouse cell line which include C-banding studies revealing the primarily heterochromatic nature of the satellite artificial chromosomes and FISH analyses showing that these satellite artificial chromosomes contain repeating units of satellite DNA. These results alone provide distinctive features of satellite artificial chromosomes readily understood by the skilled artisan. It is therefore irrelevant to a consideration of definiteness of the term "satellite artificial chromosome" whether estimates of the actual sizes of the blocks of major satellite DNA on the

megachromosomes include some "assumptions" as to the percentage of the total DNA of an endogenous mouse chromosome that is major satellite DNA. The actual particular sizes of the blocks of satellite DNA, which can only be estimated with the methods used in the Example and which may vary between different satellite artificial chromosomes, do not define a satellite artificial chromosome. Thus, the fact that the sizes of the blocks of satellite DNA were estimated in the Example referred to in the Office Action has no bearing on whether the term "satellite artificial chromosome" is definite within the context of 35 U.S.C. §112, second paragraph.

The instant application describes satellite artificial chromosomes in more than enough detail to make it clear to the skilled artisan what the term "satellite artificial chromosome" means. A particular example of a satellite artificial chromosome presented in the application is one generated using a mouse chromosome. Nonetheless, the description of satellite artificial chromosomes provided in the application applies generally and is clear and definite regardless of whether a particular specific example of a satellite artificial chromosome is a mouse, plant or other type of satellite artificial chromosome.

In alleging that "Applicant has not described plant megachromosomes," it appears that the Office Action may instead be questioning the scope, as opposed to the definiteness, of the claims. Breadth of a claim, however, is not to be equated with indefiniteness (see, *e.g.*, MPEP §2173.04 citing *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971)). Any allegation of undue claim breadth is addressed not under 35 U.S.C. §112, second paragraph, but rather under <u>different</u> statutory provisions, *e.g.*, 35 U.S.C. §112, first paragraph, or 35 U.S.C. §102 or §103. The requirements of the first and second paragraphs of 35 U.S.C. §112 are separate and distinct. As cautioned in MPEP §2174, if a description or the enabling disclosure of a specification is allegedly not commensurate in scope with the subject matter encompassed by a claim, that fact alone does not render the claim imprecise or indefinite or otherwise not in

compliance with 35 U.S.C. §112, second paragraph; rather such grounds of insufficient disclosure would instead form the basis for a rejection of the claim under 35 U.S.C. §112, first paragraph (MPEP §2174 citing *In re Borkowski*, 422 F.2d 904, 164 USPQ 642 (CCPA 1970)).

Accordingly, because the term "satellite artificial chromosome" is clear and definite, the question of the "relevance of the mouse megachromosome work to plants and plant SATACs" and the allegation of a lack of description of plant megachromosomes raised in the Office Action are improper grounds on which to base a rejection of the claims under 35 U.S.C. §112, second paragraph. It is noted that the claims are also rejected in the Office Action under 35 U.S.C. §112, first paragraph. Those rejections are addressed and traversed herein below.

The Term "Satellite Artificial Chromosome" Is Presumptively Definite Based on Use of the Term in Issued U.S. Patents

As set forth in previous responses, the instant application is a continuation-in-part of the applications upon which two U.S. patents (U.S. Patent Nos. 6,077,697 and 6,025,155) are based. Each of these patents contains claims that include the term "satellite artificial chromosome." Because an issued patent is presumed valid (35 U.S.C.§ 282), and the term "satellite artificial chromosome" is recited in the issued claims, the term "satellite artificial chromosome" is presumptively definite. Therefore, a rejection of the instant claims on the basis of an alleged indefiniteness of the term "satellite artificial chromosome" cannot be valid.

The Office Action counters this position with two statements: (1) an allegation that the instant claims are effectively drawn to plant-functional satellite artificial chromosomes which are not claimed in the patents, except for claim 27 of U.S. Patent No. 6,077,697 and (2) the Group Director of Technology Center 1600 has reviewed and signed the Office Action. It is respectfully submitted that neither of these statements provides the authority

under which the Office is permitted to disregard the presumption of validity of a U.S. Patent and now reverse its previous determination of ***definiteness*** of the claim term "satellite artificial chromosome" during *ex parte* prosecution of a continuing application containing all of the disclosure of the issued patents. Applicant is entitled to a satisfactory *explanation* as to why the disputed claim term is not ***presumptively*** definite, rather than being provided only non-responsive statements, such as one informing who is reviewing the Office Action, to which Applicant cannot respond.

Furthermore, the statement in the Office Action that "the instant claims are effectively drawn to plant-functional SATACs, which are not claimed in the patents, except claim 27 of 6,077,697" has no relevance to the issue of the presumptive definiteness of the instant claims. The rejection of the instant claims is based solely on the alleged indefiniteness of the term "**satellite artificial chromosome**." As noted above, each such rejection of the claims thus far includes the question "what is a **satellite artificial chromosome**?" As also noted above, the instant claims are not directed to "plant-functional SATACs" but instead are directed to a method for producing a transgenic plant. The method includes introducing a **satellite artificial chromosome** into a plant cell. The claim term "**satellite artificial chromosome**" is the term which is alleged to be indefinite and is the basis for the rejection of the claims under 35 U.S.C. §112, second paragraph. This term is also the term that occurs in the issued U.S. Patents.

Each of U.S. Patent Nos. 6,077,697 and 6,025,155 contains claims that include the term "satellite artificial chromosome." U.S. Patent No. 6,077,697 has 64 claims, 54 of which recite the term "satellite artificial chromosome" either directly as an independent claim or by virtue of being dependent on such an independent claim. Claim 8 of U.S. Patent No. 6,077,697 is explicitly directed to an isolated satellite artificial chromosome as a composition of matter. U.S. Patent No. 6,025,155 has 37 claims, 33 of which recite the term "satellite artificial chromosome" either directly as an independent claim or by virtue of

being dependent on such an independent claim. Accordingly, a total of 91 claims issued in these U.S. Patents effectively recite the term "satellite artificial chromosome."

Applicant has provided authority on which the position that the term "satellite artificial chromosome" is presumptively definite is based. For example, Applicant has cited 35 U.S.C.§ 282 which states that an issued patent is presumed valid. Accordingly, if a patent is presumed valid, the claims are presumed valid and the terms within the issued claims must be presumed to meet the requirements of 35 U.S.C. §112, second paragraph. It is respectfully requested that the Office apprise Applicant of the conflicting authority that would allow the Office during *ex parte* prosecution to dismiss the presumed validity of an issued patent by alleging that a term of an issued claim is indefinite and does not meet the requirements of 35 U.S.C. §112, second paragraph.

THE REJECTION OF CLAIMS 50-52 AND 73-113 UNDER 35 U.S.C. §112, FIRST PARAGRAPH - WRITTEN DESCRIPTION

Claims 50-52 and 73-113 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement for reasons of record set forth on pages 4-5 of the Office Action of 22 October 2003. In that office action, it was alleged that the satellite artificial chromosome and plant artificial chromosomes are not disclosed in the application in sufficient identifying characteristics and thus are not considered to be possessed by Applicant.

In the current Office Action, it is further stated that Applicant's traversal of this rejection is unpersuasive because: (1) Applicant's definition and description of the artificial chromosome as being a piece of DNA, but also in terms of "chromosomes," lacks at least one family of components of chromosomes: namely, proteins (*e.g.*, histone and non-histone proteins), and Applicant has provided no evidence of appropriate protein association with any

plant satellite artificial chromosomes, (2) Applicant's description of an artificial chromosome fails to distinguish it from a "wild-type" chromosome which can stably replicate and segregate alongside endogenous chromosomes "as is known from the literature, which abounds with examples of transgenic animals, fungi and plants and many progeny generations of these transgenics," (3) the deposited cells containing exemplary SATACs cannot overcome the written description rejection because the deposits are unrelated to the instant claims which are drawn to plant-functional SATACs that differ from animal SATACs in at least the presence of a plant centromere and (4) Figures 2 and 3 show schematics of a complex macromolecular pathway starting with mouse chromosome 7 being transfected with foreign DNA (specific lambda DNA) and the other components are macromolecular complexes comprising for example heterochromatin and euchromatin. Additionally, Applicant's assertion that issued patents containing claims to satellite artificial chromosomes demonstrate possession of SATACs as of the earliest filing date of the instant application is deemed unpersuasive in the current Office Action for the following reasons: (1) only one of the patented claims is drawn to plant-functional SATACs as instantly claimed and (2) the Office Action was reviewed by a PTO Director.

The rejection of the claims under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement is respectfully traversed.

RELEVANT LAW

35 U.S.C. §112, first paragraph, requires that the specification contain a written description of the invention. The test for sufficiency of support in a patent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.,* 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow,* 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)); *Vas-*

Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991); *See also* MPEP 2163.02.

There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. *In re Wertheim*, 5431 F.2d 257, 262-263, 191 USPQ 90, 96-97 (CCPA 1976) ("we are aware of the opinion that the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention as defined by the claims"). Prior to determining whether the disclosure satisfies the written description requirement for the claimed subject matter, the examiner should review the claims and **the entire specification.** Such a review is conducted from the standpoint of one of skill in the art at the time the application was filed and should include a determination of the field of the invention and the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. *See, e.g., Wang Labs v. Toshiba Corp.,* 993 F.2d 858, 865, 26 USPQ2d 1767, 1774 (Fed. Cir.1993). Information which is well known in the art need not be described in detail in the specification. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986).

The written description requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. *Capon et al. v. Eshhar et al. v. Jon Dudas,* (Fed. Cir. 2005) ("As each field evolves, this balance also evolves between what is known and what is added by each inventive contribution"). Possession may be shown in a variety of ways, including, *for example*, by (1) describing an actual reduction to practice of the claimed invention, such as, for example, a deposit of a biological material (*See, e.g., In re Lundak,* 77 3F.2d 1216, 227 USPQ 90 (Fed. Cir. 1985), (2) a clear depiction of the invention in detailed drawings or in structural chemical formulas that show the invention was complete (*See, e.g., Pfaff v. Wells Electronics, Inc.,* 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d

304, 312, 48 USPQ2d 1641, 1647 (1998) ("It is true that reduction to practice ordinarily provides the best evidence that an invention is complete. But just because reduction to practice is sufficient evidence of completion, it does not follow that proof of reduction to practice is necessary in every case. Indeed,...one can prove that an invention is complete and ready for patenting before it has actually been reduced to practice."); *Vas-Cath,* 935 F.2d at 1565, 19 USPQ2d at 1118) or (3) any description of distinguishing identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention (*See, e.g., Amgen Inc. v. Chugai Pharmaceutical,* 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991); *Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997)).

Factors to be considered in determining whether there is sufficient evidence of possession of the claimed subject matter include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed subject matter. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. (*See e.g., Regents of the University of California v. Eli Lilly,* 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998)).

ANALYSIS

The Pending Claims are Generally Directed to Methods for Producing a Transgenic Plant by Introducing a Satellite Artificial Chromosome into a Plant Cell, whereas Specific Dependent Claims Recite that the Satellite Artificial Chromosome is a Plant Satellite Artificial Chromosome

Claim 92 is the single independent claim within the currently pending claims. Claim 92 is as follows:

A method for producing a transgenic plant, comprising introducing a satellite artificial chromosome (SATAC) into a plant cell; and

growing the plant cell under conditions to produce a transgenic plant.

As noted above, claim 92, and most of the claims dependent on claim 92, involve introducing a **satellite artificial chromosome** into a plant cell. New claim 114, which is dependent on claim 92, specifies that the satellite artificial chromosome is a **plant** satellite artificial chromosome.

It is stated in the Office Action that "the instant claims are drawn to plant-functional SATACs that differ from animal SATACs in at least the presence of a plant centromere." As is clear from claim 92, this statement is not accurate. First, the claims are not drawn to compositions of matter, but rather are directed to methods for producing transgenic plants. Second, although the claimed methods include introducing a satellite artificial chromosome into a plant cell, it is not correct that "plant-functional SATACs differ from animal SATACs in at least the presence of a plant centromere." As is clear from the application, and further demonstrated by the first Declaration of Dr. Steven Fabijanski (Fabijanski Declaration 1) submitted in response to the office action mailed January 17, 2003, a satellite artificial chromosome need not necessarily be of the same "species" as the host cell into which it is introduced. For example, a mammalian satellite artificial chromosome can be transferred into a plant cell and can be detected in cells grown in culture for at least 16 weeks following such transfer (see Fabijanski Declaration 1). Thus, the claims are

generally directed to methods that include introducing a satellite artificial chromosome into a plant cell, and, in specific dependent claims, to such methods wherein the satellite artificial chromosome is a plant satellite artificial chromosome.

The Application is Replete with Detailed Descriptions of the Identifying and Distinctive Characteristics of a Satellite Artificial Chromosome, which, when Considered in View of the Level of Skill and Knowledge in the Art, Make it Clear that Applicant was in Possession of Satellite Artificial Chromosomes and Plant Satellite Artificial Chromosomes

As provided for by applicable law and restated in the "Guidelines for Examination of Patent Applications Under 35 U.S.C. §112, ¶ 1, 'Written Description' Requirement" (66 FR 4, 1099-1111 (January 5, 2001)) (hereinafter the "Guidelines for Examination under 35 U.S.C. §112, first paragraph"), possession may be shown in many ways, including, *for example*, by (1) describing an actual reduction to practice of the claimed invention, (2) a clear depiction of the invention in detailed drawings or in structural chemical formulas or (3) any description of distinguishing identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. It is respectfully submitted that possession of satellite artificial chromosomes, and plant satellite artificial chromosomes in particular, is amply demonstrated in all three of these exemplary ways by the instant application.

1. Description of a Satellite Artificial Chromosome Provided as a Biological Deposit (Actual Reduction to Practice)

First, with respect to actual reduction to practice, as noted in previous responses, the instant application describes in extraordinary detail exemplary satellite artificial chromosomes and provides deposits of cells containing exemplary satellite artificial chromosomes generated through an amplification-based method described in the application. For example, the specification describes the generation of cell lines such as G3D5 and H1D3, containing

megachromosomes (exemplary satellite artificial chromosomes) generated through amplification of mouse chromosomes. The cell lines have been deposited with the ECACC under accession nos. 96040928 and 96040929, respectively (page 74, lines 26-27 of the instant application). Thus, the application describes an actual reduction to practice of satellite artificial chromosomes.

It is alleged in the Office Action that the deposited cells containing exemplary SATACs cannot overcome the written description rejection because the deposits are unrelated to the instant claims which are drawn to plant-functional SATACs that differ from animal SATACs in at least the presence of a plant centromere. This allegation is incorrect on several bases. As a first point, it is noted again, as in previous responses submitted in connection with the examination of the instant application, that the deposited cell lines are **not** necessary to carry out the claimed methods, nor are they necessary to satisfy the written description requirement with respect to this application. The application describes satellite artificial chromosomes and the methods of making and using them (in addition to providing elaborate structural details of the exemplary satellite artificial chromosomes contained in the deposited cell lines) in more than sufficient detail to satisfy 35 U.S.C. §112, first paragraph. Reference to the deposited cell lines in this and previous responses is made to emphasize the actual reduction to practice of satellite artificial chromosomes which are thoroughly described in the application. Thus, contrary to the Office Action, the deposited cell lines are not provided to "overcome the written description rejection."

As a second point, it is noted that the Office Action rejects the claims under 35 USC §112, first paragraph, because the application allegedly fails to disclose "**satellite artificial chromosomes** *and* plant artificial chromosomes" in sufficient identifying characteristics and thus they are not considered to be possessed by Applicant. Thus, the rejection includes an allegation that satellite

artificial chromosomes generally (not just plant satellite artificial chromosomes specifically) are not considered possessed by Applicant. As such, a description and deposit of exemplary **satellite artificial chromosomes** of any type directly addresses the rejection under 35 USC §112, first paragraph.

The claimed methods likewise generally include introducing a satellite artificial chromosome into a plant cell. As is clear from the application, and further demonstrated by the first Declaration of Dr. Steven Fabijanski (Fabijanski Declaration 1) submitted in response to the office action mailed January 17, 2003, a satellite artificial chromosome need not necessarily be of the same "species" as the host cell into which it is introduced. In fact, a mammalian satellite artificial chromosome was transferred into a plant cell and could be detected in the plant cells grown in culture for at least 16 weeks following the transfer (see Fabijanski Declaration 1, and note the correction of cell line designation made in the accompanying Declaration of Fabijanski). Accordingly, contrary to the allegation in the Office Action, the description in the application of exemplary satellite artificial chromosomes and the deposit of cells containing exemplary satellite artificial chromosomes are very related to the instant claims. Clearly, the actual reduction to practice evidenced by the deposited cell lines and the extensive description of the satellite artificial chromosomes contained therein throughout the application are an irrefutable demonstration of possession of a satellite artificial chromosome at the time of filing of the application.

2. Depiction of a Satellite Artificial Chromosome in Detailed Drawings

Second, with respect to demonstrating possession through disclosure of drawings, the instant specification also depicts the structures of exemplary satellite artificial chromosomes schematically in Figures 2 and 3. In particular, a method for formation of a megachromosome is shown in Figures 2D, 2E and 2F and an exemplary megachromosome structure is depicted in Figures 2F and 3.

The drawings provided in the instant application are deemed "unpersuasive" in the Office Action because Figures 2 and 3 show schematics of a complex macromolecular pathway starting with mouse chromosome 7 being transfected with foreign DNA (specific lambda DNA) and the other components are macromolecular complexes comprising for example heterochromatin and euchromatin. It is respectfully submitted that this counterpoint raised in the Office Action is a mere statement of what the figures depict and lacks any explanation as to why the drawings are deemed "unpersuasive" of Applicant's possession of a satellite artificial chromosome at the time of filing of the application. As such, further clarification of this point is requested so that Applicant can fully address what appears to be an allegation of inadequacy of the drawings as a showing of possession of a satellite artificial chromosome.

Nonetheless, Applicant maintains that the drawings are yet further evidence of possession of a satellite artificial chromosome and a plant satellite artificial chromosome in accordance with applicable law. As set forth in the Guidelines for Examination under 35 U.S.C. §112, first paragraph, prior to determining whether the disclosure satisfies the written description requirement, the claims **and entire specification, including the specific embodiments and figures**, must be reviewed to understand how applicant provides support for the various features of the claimed subject matter. Importantly, the review is conducted from the standpoint of one of skill in the art at the time the application was filed. Thus, information which is well known in the art need not be described in detail in the specification, particularly if the level of skill and knowledge in the art is high (as it is in the case of the field of the subject matter of the instant application). The description need only describe in detail **that which is new or not conventional.**

A satellite artificial chromosome is a type of artificial chromosome. A chromosome is a macromolecule that was well-known to those of skill in the art

at the time of filing of the instant application. It was part of the knowledge of one of skill in the art that a chromosome is DNA, and that DNA is a polymer of nucleotides. The skilled artisan recognized a chromosome not by any one particular specific nucleotide sequence, but rather as a functional whole macromolecule. The specific nucleotide sequence of a piece of DNA is essentially irrelevant to the skilled artisan's understanding of a chromosome; instead, it is the functional and overall gross structural attributes of the piece of DNA that form the basis of the recognition of a chromosome by the skilled artisan.

A significant portion of the instant application is dedicated to the details of studies demonstrating that a satellite artificial chromosome is in fact an artificial type of a basic macromolecule well-known in the art: **a chromosome**. Similarly, the application provides a detailed description (including drawings) of the distinguishing identifying characteristics of this artificial chromosome. Particularly, the application presents detailed findings of the study of the architecture of the satellite artificial chromosome, with specific reference to an exemplary mouse satellite artificial chromosome generated through a thoroughly studied amplification-based process that provides great insight into the distinctive structure and physical properties of the satellite artificial chromosome. Figure 2 of the instant application shows step-by-step the amplification-based process that resulted in the generation of an exemplary satellite artificial chromosome. The figure depicts the large-scale amplification of heterochromatin that gives rise to the satellite artificial chromosome containing arrays of repeating units of duplicated DNA and more heterochromatin than euchromatin (see, in particular, the striking depiction of a satellite artificial chromosome at the bottom of Figure 2 as compared to the illustration of a typical genomic chromosome in the top, left box of the figure). Figure 3 provides a schematic representation of the architecture of an exemplary satellite artificial chromosome that serves to portray the repetitive nature of

much of the macromolecule that is reflected in the unmistakable segmented appearance of the megachromosome. Although the Figures show an exemplary satellite artificial chromosome, with a particular spacing and pattern of repeats of DNA, they apply generally to the structure and physical properties of all satellite artificial chromosomes, including plant satellite artificial chromosomes, as explained in the application. The level of detail of the Figures and the corresponding description in the application would not be possible if Applicant did not have possession of a satellite artificial chromosome at the time of filing of the application.

3. Description of Distinguishing Identifying Characteristics of Satellite Artificial Chromosomes

Third, any description in an application of distinguishing identifying characteristics of claimed subject matter whereby a skilled artisan would recognize that the inventor had possession of the subject matter is sufficient to satisfy the written description requirement. The description of satellite artificial chromosomes in the instant application, which is based on the results of exhaustive **actual** studies of satellite artificial chromosomes and the steps in the generation thereof, is extensive. For instance, Examples 4-10 of the instant application (see pp. 83-137 of the instant application) describe in elaborate detail the comprehensive analysis of satellite artificial chromosomes and the generation and functioning thereof. The Examples recount in-depth studies that provided a level of detail of the characteristics of satellite artificial chromosomes that far surpasses the amount of description required to demonstrate Applicant's possession of a satellite artificial chromosome. To vivify this point, some of the description provided in the Examples can be highlighted as follows:

•Example 4 describes the sausage chromosome that formed during generation of satellite artificial chromosomes as a stable chromosome with a ~100-150 Mb heterochromatic arm composed of four to five satellite segments rich in satellite DNA, and evenly spaced integrated heterologous "foreign" DNA sequences. The Example details the FISH analysis of the sausage chromosome that elucidated the presence of integrated heterologous DNA interspersed in mouse major satellite DNA,

the main component of the mouse pericentric heterochromatin, and revealed **the banding pattern of the heterochromatic arm that is characteristic of the heterochromatic arms of a satellite artificial chromosome**. The analysis of the sausage chromosome further revealed that the foreign genes (encoding hygromycin resistance and β-galactosidase) located within the heterochromatic arm were highly expressed (as determined by LacZ staining and growth of the sausage chromosome-containing cells on hygromycin).

•Example 6 describes the generation and painstaking analysis of the satellite artificial chromosome referred to as the megachromosome. The Example explains that in cells containing a sausage chromosome, a further amplification was observed in which, in addition to the ~100-150 Mb heterochromatic arm of the sausage chromosome, an extra centromere and a ~150-250 Mb heterochromatic chromosome arm were formed, which differed from those of mouse chromosome 7. By the acquisition of another euchromatic terminal segment, a new submetacentric chromosome (megachromosome) was formed. Example 6 describes the exhaustive analyses conducted to elucidate the fine details of the structure of the satellite artificial chromosome, including G-banding and in situ hybridization studies. The results of these analyses are also provided, and revealed that, apart from the euchromatic terminal segments, the whole megachromosome is constitutive heterochromatin. The hybridization results revealed a segmented pattern of the megachromosome resulting from tandem arrays of at least 40 [~7.5 Mb] blocks of mouse major satellite DNA [see Figures 2 and 3]. Four satellite DNA blocks are organized into a giant palindrome [amplicon] carrying integrated exogenous DNA sequences at each end. The long and short arms of the submetacentric megachromosome contains 6 and 4 amplicons, respectively. Hybridization with a mouse minor satellite probe (specific to the centromeres of mouse chromosomes) showed a strong hybridization signal that was detected only at the primary constriction of the megachromosome, thereby confirming the presence of a single centromere within the megachromosome. A striking structural regularity in the megachromosome was also detected using FPG staining of the megachromosome. In both chromatids, alternating dark and light staining that produced a checkered appearance of the megachromosome was observed. Example 6 also describes large-scale mapping of megachromosome DNA by pulsed-field electrophoresis and Southern hybridization with foreign DNA probes and endonuclease treatment which revealed a simple pattern of restriction fragments indicative of the homogeneity of DNA in the amplified segments. **The homogeneous architecture of the heterochromatic arms of the megachromosome** was confirmed by high resolution scanning electron microscopy whereas the centromeres showed a more compact, finely fibrous appearance than the surrounding heterochromatin.

•Example 8 describes analyses (and the actual results thereof) of replication of an exemplary satellite artificial chromosome by BrdU pulse labelling followed by immunolabelling. The replication patterns and the sequence of replication of an exemplary megachromosome are described down to the point of identifying the locations of the sites of replication initiation, measurement of the total replication time for the heterochromatic regions, and the timing of events within the cell cycle. As set

forth in the application, these elegant studies take advantage of the **heterochromatic nature** of the satellite artificial chromosome to elucidate the process of replication of constitutive heterochromatin.

•Example 10 describes in detail methods for isolating satellite artificial chromosomes, such as by fluorescence activated cell sorting [FACS]. This method takes advantage of the nucleotide base content of the SATACs, **which by virtue of their heterochromatic content** will differ from any other chromosomes in a cell. In particular, metaphase chromosomes are isolated and stained with base specific dyes, such as Hoechst 33258 and chromocycin A3. Fluorescence activated cell sorting separates the SATACs from the genomic chromosomes. Because of the difference between the base composition of the satellite artificial chromosomes and the other chromosomes and the resulting difference in interaction with the dyes, as well as size differences, the artificial chromosomes were separated from the other chromosomes.

There are over **30 pages** of description of the identifying characteristics of satellite artificial chromosomes, including methods of generating and isolating the artificial chromosomes, obtained from countless hours of **actual experimental studies** contained in the aforementioned Examples alone. The experimental results repeatedly reflect the primarily heterochromatic structure of the artificial chromosomes and the repetitive DNA content occurring from duplication of the DNA in the amplification process that make these artificial chromosomes so easily identified and distinguished from typical "wild-type" chromosomes in cells. It is difficult to reconcile the allegation in the Office Action that the "Applicant's description of an artificial chromosome fails to distinguish it from a 'wild-type' chromosome..." with a proper reading and assessment of the **entire specification and drawings as a whole** as is so clearly required by the Guidelines for Examination under 35 U.S.C. §112, first paragraph. After all, as described in the application, it was the distinctive properties of these artificial chromosomes that formed the basis of their discovery within the context of a cell containing "wild-type" chromosomes and that allow for so much of the detailed analysis of the artificial chromosomes (*e.g.*, isolation from endogenous "wild-type" chromosomes, replication of constitutive heterochromatin, etc.). The amount and level of detailed information about the satellite artificial

chromosomes provided in the Examples and throughout the application are far beyond that required to satisfy the written description requirement.

In view of the abundance of information provided in connection with the description of the distinguishing and identifying characteristics of satellite artificial chromosomes, it is essentially unimaginable that a person skilled in the art would have any doubt whatsoever that the inventor had possession of satellite artificial chromosomes. Not only does the application demonstrate possession in *one* of the several exemplary ways suggested by the Guidelines for Examination under 35 U.S.C. §112, first paragraph (based on established law), it demonstrates possession in **all** of the exemplary ways. Further, an assessment of the factors to be considered in determining whether there is sufficient evidence of possession of claimed subject matter also leads to the clear conclusion that the application satisfies the requirements of 35 U.S.C. §112, first paragraph: (1) the level of skill and knowledge in the art is high, (2) the full and distinctive structure of a satellite artificial chromosome (including two arms containing extensively duplicated DNA segments and a centromeric constriction) is described and depicted in drawings, (3) the distinguishing physical properties, such as the primarily heterochromatic nature of the artificial chromosomes, are elaborated, (4) the chemical properties of DNA in general are well-known in the art, (5) the functional characteristics of satellite artificial chromosomes (*e.g.*, replication, segregation and maintenance within cells, high-level expression of coding sequences contained within) which are correlated to its structure as a chromosome are demonstrated through actual experimental results, and (6) methods of making satellite artificial chromosomes are outlined in step-by-step detail. Applicant respectfully urges that the application and figures be reviewed as a whole and requests that the question of how such an elaborate description, including figures and descriptions of actual reduction to practice of satellite artificial chromosomes, could possibly fail to demonstrate possession be <u>directly</u> addressed if this untenable rejection is maintained.

4. The Description of the Common Attributes Possessed by Satellite Artificial Chromosomes as a Genus Applies to Plant Satellite Artificial Chromosomes which are Further Described in Terms of Their Specific Relevant Identifying Features

The written description requirement may be satisfied for a genus, such as the genus of satellite artificial chromosomes, in a number of ways, including through description of species (*e.g.*, description of actual reduction to practice, drawings) or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see the Guidelines for Examination under 35 U.S.C. §112, first paragraph). As explained above, the description of satellite artificial chromosomes in the instant application demonstrates possession of the genus through all of the exemplary ways cited in the Guidelines for Examination under 35 U.S.C. §112, first paragraph.

As also set forth in the Guidelines for Examination under 35 U.S.C. §112, first paragraph, a description of an actual reduction to practice of a particular species is but one of many ways to satisfy the written description requirement and is by no means necessary to satisfy the requirement. *See, e.g., Pfaff v. Wells Electronics, Inc.,* 55 U.S. at 66, 119 S.Ct. at 311, 48 USPQ2d at 1646 (1998) ("...just because reduction to practice is sufficient evidence of completion, it does not follow that proof of reduction to practice is necessary in every case. Indeed,...one can prove that an invention is complete and ready for patenting before it has actually been reduced to practice.") Additional ways to demonstrate satisfaction of the written description requirement with respect to a particular species include a description of the claimed subject matter in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed subject matter. Factors to consider include (1) the

level of skill and knowledge in the art, (2) partial structure, (3) physical and/or chemical properties, (4) the functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and (6) the method of making the claimed subject matter.

The Application Describes Plant Satellite Artificial Chromosomes in Terms of Distinguishing Identifying Characteristics as Evidenced by Other Descriptions of Satellite Artificial Chromosomes

The description of satellite artificial chromosomes in the instant application amply demonstrates possession of a plant satellite artificial chromosome in many ways consistent with the tests set forth in the Guidelines for Examination under 35 U.S.C. §112, first paragraph. First, the application provides a detailed description of the common features of satellite artificial chromosomes that applies whether the satellite artificial chromosome is derived from an animal, plant or other cell. The application makes clear that the common attributes possessed by the members of the genus of satellite artificial chromosomes are relatively invariant: they have more heterochromatin than euchromatin and generally contain duplicated sègments of DNA, which typically include highly repetitive DNA, such as, for example, pericentric heterochromatic DNA or satellite DNA. Although unnecessary for satisfaction of the written description requirement (An inventor does not need to know how or why the invention works in order to obtain a patent, see, *e.g.*, *Newman v. Quigg,* 877 F.2d 1575, 1581, 11 USPQ 1340, 1345 (Fed. Cir. 1989)), the application explains that these common attributes of satellite artificial chromosomes are likely the result of amplification of heterochromatic DNA, which is a phenomenon generalizable to chromosomes. Thus, although the particular DNA sequences and amplified chromosome segments within different satellite artificial chromosomes may differ at the nucleotide and substructural level, these artificial chromosomes share similarities as a whole that distinguish and identify them as satellite artificial chromosomes.

Consideration of Factors Relevant to a Determination of Satisfaction of the Written Description Requirement Further Evidence Possession of Plant Satellite Artificial Chromosomes

As established in previous responses submitted in connection with examination of the instant application, the level of skill and knowledge in the art is high. The skilled artisan, upon reading the description of satellite artificial chromosomes provided in the instant application would readily recognize that Applicant was in possession of plant satellite artificial chromosomes.

First, the structure of a plant satellite artificial chromosome is clear from the description in the instant application. The application explains that plant satellite artificial chromosomes are **satellite artificial chromosomes** that include plant centromeres (see, *e.g.*, page 16, lines 18-25, of the instant application), and that the methods for producing satellite artificial chromosomes are applicable to any higher eukaryotic cell, including, *e.g.*, mammals, insects and plants. Clearly, as set forth in detail above, a satellite artificial chromosome in general, and as particularly exemplified with respect to mammalian satellite artificial chromosomes actually reduced to practice, is more than sufficiently described in the application. The application describes how a satellite artificial chromosome may be generated from any cell, including a mouse cell and a plant cell, through amplification of heterochromatin contained in the cell's chromosomes, *e.g.*, a mouse or a plant chromosome. The application describes the structural details of a satellite artificial chromosome (*e.g.*, as exemplified by a mouse satellite artificial chromosome actually reduced to practice) and the distinguishing physical characteristics that identify a satellite artificial chromosome. One of skill in the art could immediately envisage from the instant application a plant satellite artificial chromosome as a chromosome (**a structure well-known in the art as containing DNA of known chemical properties**) in the characteristic form of two arms extending from a constricted region of plant centromeric DNA (as may be obtained from a chromosome in a plant cell

analogous to the obtaining of mammalian centromeric DNA from a chromosome in a mouse cell) containing more heterochromatin than euchromatin. Certainly the level of skill and knowledge in the art is such that skilled artisan can identify and distinguish animal and plant cells and, further, can determine through structural and functional analyses if a satellite artificial chromosome contains a centromere. Additionally, the skilled artisan would understand the correlation between the functional aspects of the plant satellite artificial chromosome (*e.g.*, replication and maintenance in plant cells) and the described structure of the plant artificial chromosome.

In accordance with the Guidelines for Examination under 35 U.S.C. §112, first paragraph, the disclosure of the combination of these factors (structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, the method of making plant satellite artificial chromosomes, and the level of skill in the art) distinguishes plant satellite artificial chromosomes from other materials and would lead one of skill in the art to the conclusion that Applicant was in possession of plant satellite artificial chromosomes. As such, the application provides an adequate written description of plant satellite artificial chromosomes.

This conclusion is underscored by the fact that the description of a plant satellite artificial chromosome provided in the instant application identifies the actual physical embodiment of a plant satellite artificial chromosome generated using methods described in the application (see methods and results provided in Fabijanski Declaration 2 filed April 22, 2004). Fabijanski Declaration 2 describes the results of analyses of calli obtained by PEG-mediated transfection of tobacco protoplasts with heterologous DNA. Through those analyses, which included fluorescence in situ hybridization (FISH) for visualization of pericentric heterochromatin and the heterologous DNA, it was possible to identify a plant satellite artificial chromosome based on the description of a plant satellite

artificial chromosome in the instant application. As set forth in Fabijanski Declaration 2, the plant satellite artificial chromosome was clearly visible in chromosome spreads as a small independent chromosome entity containing amplified heterologous DNA and pericentric DNA. Metaphase images of the plant satellite artificial chromosome demonstrated the presence of small chromosome arms and a constriction representing the centromere region containing plant centromeric DNA. A comparison of DAPI-stained chromosomes from calli generated from the transfected protoplasts and the results of FISH analyses of the same chromosomes using a FITC-labeled probe specific for a portion of the heterologous DNA (*i.e.*, a mouse major satellite DNA sequence) and a rhodamine red-labeled probe specific for tobacco pericentric heterochromatin (*i.e.*, 18S rDNA) further revealed that the entire plant satellite artificial chromosome hybridized to the 18S rDNA-specific probe (see Figure 2 (A) and (C) of the accompanying Declaration of Fabijanski (Fabijanski Declaration 4). Additionally, significant hybridization of the heterologous DNA-specific probe to the plant satellite artificial chromosome (see Figure 2 (A) and (B) of Fabijanski Declaration 4) reveals the co-amplified heterologous DNA contained within the artificial chromosome. Thus, as described in the instant application, the plant satellite artificial chromosome is predominantly heterochromatin (*i.e.*, rDNA) with interspersed heterologous DNA. This is particularly evident in an overlay of the FITC-labeled and rhodamine-labeled image analyses of the plant satellite artificial chromosome (see Figure 3 of Fabijanski Declaration 4). The callus line containing the plant satellite artificial chromosome was stably maintained in culture for well over six months (see Fabijanski Declaration 2), thereby demonstrating the correlation between the function (replication and stable maintenance in cells) and structure of the plant satellite artificial chromosome as described in the instant application. Clearly, the description of a plant satellite artificial chromosome provided in the instant application is one that describes the plant satellite artificial chromosome

depicted in the accompanying Declaration of Fabijanski (Fabijanski Declaration 4) and Fabijanski Declaration 2. Thus, there can be no doubt that plant satellite artificial chromosomes are sufficiently described in the instant application to demonstrate Applicant's possession of these artificial chromosomes.

A Consideration of the Types of Molecules (*e.g.*, Proteins) that May or May Not Associate with a Satellite Artificial Chromosome is Not Relevant to the Determination of the Sufficiency of the Description in the Application in Demonstrating Whether Applicant was in Possession of Satellite Artificial Chromosomes

It is alleged in the Office Action that the Applicant's description of an artificial chromosome as DNA is lacking at least one family of components - the proteins (e.g., histone and non-histone proteins) - and that Applicant has provided no evidence of appropriate protein association with any plant satellite artificial chromosome. It is respectfully submitted that a description of proteins that may be associated with a satellite artificial chromosome is unnecessary to demonstrate possession of a satellite artificial chromosome with respect to satisfying the requirements of 35 U.S.C. §112, first paragraph. Characterization of protein that may be associated a satellite artificial chromosome in any particular state within in a cell or in isolation does not contribute to the description of the **relevant identifying** characteristics providing evidence that Applicant was in possession of an artificial chromosome. It is generally known in the art that DNA typically is not "naked" within a cell and at any particular time may be associated with different other types of molecules. However, these molecules do not define a particular type of chromosome. Studies and descriptions of chromosomes in the art are based on an analysis of the nucleic acid-related structure of chromosomes, just as are many of the studies of satellite artificial chromosomes presented in the instant application. By way of analogy, it is possible to have possession of and claim a cell without describing each of the components (*e.g.*, the proteins) of the cell. To satisfy the requirements of 35 U.S.C. §112, first paragraph, an applicant need only provide

a description of **sufficient, relevant, identifying** characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed subject matter as a whole. The description need only describe in detail that which is new or not conventional.

Clearly, as explained above, the description of the relevant, identifying characteristics of satellite artificial chromosomes, including satellite artificial chromosomes actually reduced to practice, provided in the instant application is irrefutable evidence of Applicant's possession of these artificial chromosomes. The application describes the detailed distinguishing characteristics of satellite artificial chromosomes and further describes the replication and maintenance of satellite artificial chromosomes in cells, the purification of the artificial chromosomes from the endogenous chromosomes of a cell, the transfer of the artificial chromosomes between and into cells, and the expression of protein-encoding DNA within the satellite artificial chromosomes. A description of proteins or evidence of protein association with a plant satellite artificial chromosome as suggested in the Office Action is simply unnecessary to a demonstration of possession of satellite artificial chromosomes.

The Description of Satellite Artificial Chromosomes in the Instant Application Is Presumptively Adequate in Satisfaction of the Requirements of 35 U.S.C. §112, First Paragraph, Based on Adequacy of the Same Description in Issued U.S. Patents

As noted above in rebutting the rejection of the claims under 35 U.S.C. §112, second paragraph, the instant application is a continuation-in-part of the applications upon which two U.S. patents (U.S. Patent Nos. 6,077,697 and 6,025,155) are based. The entire disclosure of the parent applications that gave rise to the two U.S. Patents is contained within the instant application. Each of these patents contains claims that include the term "satellite artificial chromosome." Because an issued patent is presumed valid (35 U.S.C.§ 282), and satellite artificial chromosomes are included in the subject matter of the issued claims, the description of satellite artificial chromosomes in the patents is

presumptively adequate to satisfy the requirements of 35 U.S.C. §112, first paragraph. Therefore, a rejection of the instant claims on the basis of an alleged failure to comply with the written description requirement because satellite artificial chromosomes are not disclosed in the application in sufficient identifying characteristics to be considered to be possessed by Applicant cannot be valid.

The Office Action counters this position with two statements: (1) an allegation that the instant claims are effectively drawn to plant-functional satellite artificial chromosomes which are not claimed in the patents, except for one claim and (2) the Group Director of Technology Center 1600 has reviewed the Office Action. As also noted above, however, neither of these statements provides the authority under which the Office is permitted to disregard the presumption of validity of a U.S. Patent and now reverse its previous determination of ***adequacy*** of the description of satellite artificial chromosomes during *ex parte* prosecution of a continuing application containing all of the disclosure of the issued patents. Applicant is entitled to a satisfactory *explanation* as to why the description does not ***presumptively*** satisfy the requirements of 35 U.S.C. §112, first paragraph, rather than being provided only non-responsive statements, such as one informing who is reviewing the Office Action, to which Applicant cannot respond.

Furthermore, the statement in the Office Action that "the instant claims are effectively drawn to plant-functional SATACs, which are not claimed in the patents, except for one claim, has no relevance to the issue of the presumptive adequacy of the description of satellite artificial chromosomes in the instant application. The rejection of the instant claims is based on the alleged failure of the instant application to comply with the written description requirement because **satellite artificial chromosomes** and plant satellite artificial chromosomes are not disclosed in the application in sufficient identifying characteristics." Because the rejection alleges insufficiency of the description of

a satellite artificial chromosome, which is the subject matter of claims issued in two U.S. Patents, the presumptive adequacy of the description of satellite artificial chromosomes in the instant application is quite germane to the rebuttal of the rejection.

Applicant has provided authority on which the position that the description of a satellite artificial chromosome in the instant application is presumptively adequate is based. For example, Applicant has cited 35 U.S.C. § 282 which states that an issued patent is presumed valid. Accordingly, if a patent is presumed valid, the claims are presumed valid and the description of subject matter within the issued claims must be presumed to meet the requirements of 35 U.S.C. §112, first paragraph. It is respectfully requested that the Office apprise Applicant of the conflicting authority that would allow the Office during *ex parte* prosecution to dismiss the presumed validity of an issued patent by alleging that the patent's description of subject matter within the issued claims is insufficient to demonstrate possession of the subject matter and does not meet the requirements of 35 U.S.C. §112, first paragraph.

THE REJECTION OF CLAIMS 50-52 AND 73-113 UNDER 35 U.S.C. §112, FIRST PARAGRAPH - ENABLEMENT

Claims 50-52 and 73-113 are rejected under 35 U.S.C. §112, first paragraph, in part for reasons of record as set forth in the office action mailed October 22, 2003 (pp. 6-8) and, furthermore, due to the alleged unpredictability inherent in obtaining transformed plant cells as claimed. The claims are described in the Office Action as broadly reading on any transformed plant of any of a multitude of unrelated species, and, in particular, on a multitude of recalcitrant monocotyledonous species (claims 88-91, 94 and 98-99). However, Ohgawara *et al.* (1983) and Potrykus (1990) are alleged to demonstrate the unpredictability inherent in liposome-mediated plant transformation (claims 52, 75, 82, 102 and 109) and in plant transformation and maintenance of exogenous DNA in plants as generally claimed, particularly

in monocots (claims 88-91, 94 and 98-99). Thus, it is concluded in the Office Action that the application "is not enabled for the claimed invention as commensurate in scope with the claims" since the specification allegedly does not provide any teachings of plant transformation of any species which would be required to overcome the evidence of unpredictability inherent in obtaining transformed plant cells as claimed.

Additionally, the Declaration of Fabijanski submitted with the Preliminary Amendment on January 6, 2005 (Fabijanski Declaration 3), which is described as providing information of the production of a plant SATAC and transgenic tobacco plants containing the plant SATAC, is alleged in the Office Action as not being supported by the specification as of the date of filing. Specifically, it is alleged that (1) Fabijanski employs information and biological materials not available as of the earliest filing date (April 1996), (2) the method employed in Fabijanski Declaration 3 uses two different constructs in step 1 and (3) the specification describes in vitro construction of artificial chromosomes, but this is not the method set forth in Fabijanski Declaration 3.

The rejection is respectfully traversed.

Scope of the Claims

The claims are directed to methods for producing a transgenic plant by introducing a satellite artificial chromosome into a plant cell and growing the plant cell under conditions to produce a transgenic plant. The dependent claims specify particular types of plant cells or protoplasts, that the satellite artificial chromosome is a plant satellite artificial chromosome, and/or comprises heterologous DNA that encodes a gene product, and/or particular methods for the introduction of the satellite artificial chromosomes into plant protoplasts.

Plant Transformation is not Unpredictable

It is alleged in the Office Action that liposome-mediated plant transformation, and plant transformation and maintenance of exogenous DNA in plants generally, and in monocots particularly, are inherently unpredictable. To

support these allegations, the Office Action relies on Ohgawara *et al.* [(1983) *Protoplasma 116*:145-148] and Potrykus [(1990) *Bio/Technology 8*:535-542]. Contrary to the assertions in the Office Action, at the time of filing of the priority application (*i.e.*, April 10, 1996) on which the instant application is based, plant transformation was not unpredictable.

The Ohgawara *et al.* Reference

First, it is respectfully submitted that the characterization in the Office Action of the information presented by Ohgawara *et al.* is inaccurate. The cited reference does not demonstrate "unpredictability inherent in liposome-mediated plant transformation" as asserted in the Office Action; rather, the reference shows predictable liposome-mediated transfer of plasmid DNA into protoplasts but limited plasma stability in plant cells over prolonged periods of time. Ohgawara *et al.* report the results of a kinetic analysis of liposome-mediated transfer of plasmid DNA (pBR322 or pBR325) into *Daucus carota* protoplasts. Specifically, it was determined that the maximum uptake of liposome-DNA was approximately 10 minutes and that approximately 50% of the DNA taken up by the protoplasts was associated with the nuclear subcellular fraction after 15 minutes of incubation. Additionally, Ohgawara *et al.* report results of Southern hybridization studies of the DNA in the nuclear fraction of protoplasts (*D. carota*, *V. rosea* and *N. glutinosa*) treated with liposome-pBR325 DNA followed by culture for 20 hours and for 1 week. Those results revealed that no covalently closed form of the plasmid was detected after 20 hours in culture (only open circular and complexed forms of pBR325) and that after 1 week in culture, only a trace amount of plasmid DNA was detected and only in *D. carota* protoplasts. The authors conclude that it is unlikely that bacterial plasmid ever replicates in plant cells in long-term culture. Thus, while the liposome-mediated transfer of heterologous DNA into the plant cells was predictable, the ***stability*** of the **plasmid** DNA in prolonged culture was found to be limited. In fact, the authors express a hope that "the application of recombinant technology will

provide in the future such vectors as capable of replicating in plant cells" (last sentence on p. 147 of Ohgawara *et al.*).

Indeed, as described in the instant application and further demonstrated by the data presented in each of the Fabijanski Declarations submitted thus far, satellite artificial chromosomes replicate and are stable in plant cells and transgenic plants for extended time periods. For example, Fabijanski Declaration 1 describes the transfer of a mammalian satellite artificial chromosome into tobacco and Arabidopsis protoplasts by microcell-mediated fusion and into rice protoplasts by cationic lipid-mediated and detection of the artificial chromosomes in the transfected protoplasts for 8-16 weeks thereafter. Fabijanski Declaration 2 describes the generation of a plant satellite artificial chromosome in tobacco protoplasts and detection of the satellite artificial chromosome in resulting calli for over six months. Fabijanski Declaration 3 describes the generation of transgenic tobacco and transgenic hybrid (resulting from fusion of *N. tabacum* and *N. glauca* protoplasts) plants containing plant satellite artificial chromosomes. Thus, as described in the instant application, satellite artificial chromosomes are stable, replicating chromosomal vectors that overcome many of the limitations of plasmid DNA. Thus, instead of serving as a demonstration of unpredictability of liposome-mediated plant cell transformation, the Ohgawara *et al.* reference emphasizes one of the problems of plasmid DNA that is overcome by satellite artificial chromosomes.

The Potrykus Reference

It is alleged in the Office Action that the Potrykus reference demonstrates unpredictability inherent in plant transformation and maintenance of exogenous DNA in plants, particularly monocots, due to the general recalcitrance of monocots to transformation, variables that affect recovery of transgenic plants and the assertion that of 23 different plant transformation techniques, only 2 (direct gene transfer and microprojectile bombardment) have shown any promise in producing transformed monocots. It is respectfully

submitted, however, that recalcitrance to transformation and a finite number of different techniques that work efficiently to transform monocots are not synonymous with unpredictability of plant transformation.

First, it is noted that the Potrykus reference is limited to a review of gene transfer to **cereals**. While cereals include several monocotyledonous species, there are many monocots that are not cereals. Second, the author clearly admits that the discussion provided in the reference is "necessarily subjective, framed within a rigid definition of what constitutes proof of gene integration, and the biological factors affecting transformation and competence...the assessment will be subjective...and several statements will be made for which no solid experimental data are available" (see p. 535 of the Potrykus reference). Third, while the reference points to several transformation methods (*e.g.*, *Agrobacterium*, viral vectors, pollentube pathway, liposome injection, biolistics/particle gun, microinjection, electroporation) that purportedly, at that time, had not provided for transgenic cereal, it also refers to methods (*e.g.*, direct gene transfer into protoplasts, liposome fusion with tissues and protoplasts), that were successful in yielding transgenic cereal. Furthermore, the Potrykus reference describes Raineri *et al.* as presenting "three lines of evidence giving a reasonable inference of *Agrobacterium*-mediated transformation of rice (*Oryza Sativa*)" and notes that definitive proof should be relatively straightforward to obtain (see page 538, paragraph numbered "3" of the Potrykus reference). While the citation is not provided in the reference, it appears that it is as follows: Raineri *et al.* (1990) *Bio/Technology 8*:33-38 (a copy of which is provided with the information disclosure statement and Form PTO-1449 being submitted with this Response). Additionally, in the note added in proof (see page 542 of the Potrykus reference), the author refers to the recent establishment of proof of the recovery of transgenic offspring of *Indica* type rice (it appears that this success is reported in Ghosh Biswas *et al.* (1994) *J. Biotechnol. 15*:1-10 which describes PEG-mediated transformation of

protoplasts from meristematically active, embryogenic cell suspension lines; note that the last author of Ghosh-Biswas *et al.* is I. Potrykus). (A copy of Ghosh Biswas *et al.* is provided with the information disclosure statement and Form PTO-1449 being submitted with this Response.)

Importantly, it is noted that the Potrykus reference was published in 1990, and the effective filing date of the above-referenced application is April 10, 1996. Thus, the Potrykus reference, published in 1990, does not reflect the state of the art in 1996. For example, Vain *et al.* [(1995) *Biotechnol. Adv. 13*:653-671] (a copy of which is provided with the information disclosure statement and Form PTO-1449 being submitted with this Response) provides a review of gene transfer into monocotyledonous species that includes the development of transgenic monocots in the years after 1990 and prior to 1996. It is concluded in Vain *et al.* that as of 1995, "at least one genotype of each major monocotyledonous crop species, including cereals, can be genetically transformed." Tables 1-3 in Vain *et al.* list numerous references of transformation of monocots. Table 3, in particular, lists numerous references describing transformation of monocots using particle gun technologies that are referred to as having "revolutionized genetic transformation of monocotyledonous species" since 1990. Vain *et al.* also points out that at least 120 field trials of genetically engineered monocots have been reported as of 1995 (see Ahl Goy and Duesing (1995) *Bio/Technology 13*:454-458; a copy of which is provided with the information disclosure statement and Form PTO-1449 being submitted with this Response). Vain *et al.* does state that the most efficient techniques for delivery of foreign genes to monocots are based on direct DNA transfer, which frequently results in the integration of numerous intact or modified copies of a transgene in the plant genome within a limited number of loci. The reference thus concludes that the further evolution of monocot transformation technologies appears to depend on the development of techniques that allow controlled integration and expression of foreign DNA into

the plant genome (see page 662 of Vain *et al.*). Therefore, as was the case with the Ohgawara *et al.* reference, Vain *et al.* emphasizes one of the challenges of genetic transformation of plants that is overcome by the stable autonomous replication of satellite artificial chromosomes.

In summary, the references relied on in the Office Action to demonstrate unpredictability of transformation of plants (particularly monocots), do not support such an assertion and further do not reflect the state of the art on the effective filing date of the instant application. While monocots may not be readily susceptible to delivery of foreign DNA by *all* possible techniques, and some species may be more recalcitrant than others, the fact that there were successful methods of monocot transformation available and well known to the skilled artisan in 1996 makes it clear that transformation of many (even if not all) monocots using some (if not all) techniques was not unpredictable. Furthermore, one of the apparent challenges in plant transformation at the effective filing date was stable maintenance of foreign DNA in transformed plants which, as described in the instant application, and further demonstrated in the Fabijanski Declarations, is overcome by use of satellite artificial chromosomes.

The Declaration of Fabijanski dated December 7, 2004 (Fabijanski Declaration 3) Demonstrates Generation of a Transgenic Plant as Described in the Instant Application

Fabijanski Declaration 3 Is Supported by the Specification as of its Effective Filing Date

It is asserted in the Office Action that although Fabijanski Declaration 3, which was submitted in connection with the response filed January 6, 2005, provides information of the production of a plant satellite artificial chromosome and of transgenic tobacco plants containing the satellite artificial chromosome, it is not supported by the specification as of the date of filing. Specifically, it is alleged that the methods described in Fabijanski Declaration 3 employ information (Borisjuk *et al.* (1997) *Plant Mol. Bio. 35*:655-660) and biological

materials (*e.g.*, DNA sequences of Genbank Accession no. X76056; see Genbank Accession no. Y08422) not available until after the filing date. The Office Action particularly states that Genbank accession no. X76056 was not available until September 27, 1996, at the earliest.

It is respectfully requested that the source of the date information for Genbank accession no. X76056 accessibility relied on in the Office Action be clarified. A review of the Genbank information for accession no. X76056 reveals that it was first seen at NCBI on July 17, 1994, at 12:40 a.m. (see accompanying Exhibit A which is a print-out from PubMed showing revision history for accession no. X76056). This sequence is for the rDNA intergenic spacer of *Nicotiana sylvestris* and is very closely related (approximately 87% sequence identity) to that of the rDNA intergenic spacer sequence of *Nicotiana tabacum* (discussed in the Borisjuk *et al.* reference which corresponds to accession no. Y08422 which was first seen on NCBI on October 8, 1996). Additionally, *N. tabacum* rDNA intergenic spacer nucleotide sequence was also available through NCBI beginning on October 25, 1995, as accession no. D76443 (see accompanying Exhibit B which is a print-out from PubMed showing revision history for accession no. D76443). Thus, contrary to the Office Action, the tobacco rDNA intergenic spacer sequence to which the 334-bp sequence in pAgIIa has homology was available on the effective filing date (i.e., April 10, 1996) of the instant application. Also at that time, it was known that rDNA was a part of the pericentric heterochromatin in plants. Thus, the use of this pericentric rDNA sequence in connection with generation of a plant satellite artificial chromosome is consistent with the teachings of the instant application, which states that the DNA that is introduced into a plant cell in the process of generating a plant satellite artificial chromosome can include sequences that target it to the pericentric region of the chromosome.

Furthermore, as discussed in the accompanying Declaration of Fabijanski (Fabijanski Declaration 4), a 1.7-kb sequence with homology to plant pericentric

DNA (*i.e.*, the 26S rDNA coding region of *Arabidopsis*; Genbank accession no. X52320) was introduced on a vector separate from pAgIIa (containing selectable and detection markers) into the tobacco protoplast in the method of generating the plant satellite artificial chromosome for convenience in providing a large molar excess of it relative to pAgIIa. Use of such "targeting" DNA in generating a satellite artificial chromosome is taught in the instant application. As described in the above-captioned application, large-scale amplification that gives rise to satellite artificial chromosomes can be induced by insertion of heterologous DNA into the pericentric DNA; thus, to enhance the occurrence of such integration, the heterologous DNA introduced into a recipient cell can contain sequence homologous to pericentric DNA for "targeted" homologous recombination. As is generally known in the art however, the smaller the region of homology to a specific region of a chromosome that an exogenous DNA introduced into a cell has, the lesser efficiency of homologous recombination will be between the exogenous DNA and the homologous portion of an endogenous chromosome. Furthermore, the smaller the amount of an exogenous DNA that is introduced into a cell for homologous recombination therein, the lesser the frequency of integration into the homologous portion of an endogenous chromosome.

Data presented in Fabijanski Declaration 3 (which are also presented in Fabijanski Declaration 4) illustrate that reducing the excess of targeting DNA (*i.e.*, DNA with homology to pericentric DNA) similarly reduces the efficiency of integration of the exogenous DNA into the pericentric heterochromatin and thereby reduces large-scale amplification of the DNA. Furthermore, the Declarations compare the results of the transfections using pAgIIa (which contains a small 334 bp region homologous to a portion of the tobacco rDNA repeat structure) and an excess of DNA containing a larger region (*i.e.*, 1.7 kb) of homology to pericentric DNA with the results of transfections using pAgIIa without an excess of such DNA (*i.e.*, using salmon sperm or calf thymus DNA)

which demonstrate that an excess of a larger sequence with homology to pericentric DNA provides for more efficient homologous recombination than a lesser amount of a smaller homologous sequence. These basic strategies for increasing the efficiency of homologous recombination were widely practiced and well within the knowledge of the skilled artisan at the effective filing date of the instant application.

Nonetheless, as explained in accompanying Declaration of Fabijanski, it is likely that analyses of a greater number of tobacco protoplasts that were transfected with pAglla and the other DNA (*i.e.*, salmon sperm or calf thymus DNA) and thus without the additional 1.7-kb sequence in the "targeting DNA" would have yielded an amplification event resulting in a plant satellite artificial chromosome. Only eight such transfectant calli were analyzed; due to the lower efficiency of targeted integration that occurs without a molar excess of DNA homologous to pericentric DNA, a greater number would need to be observed in order to find a satellite artificial chromosome.

It is also remarked in the Office Action that "surely [in vitro artificial chromosome construction] is not the method of Fabijanski set forth in Fabijanski Declaration 3." The Office Action is correct. The instant application describes multiple methods for generating a satellite artificial chromosome. The method used in generating the plant satellite artificial chromosome described in Fabijanski Declaration 3 is described in detail in the instant application but is not the in vitro method.

THE REJECTION OF CLAIMS 50-52, 73, 80 88-92, 94-96, 98-100 AND 107 UNDER 35 U.S.C. §102

Claims 50-52, 73, 80, 88-92, 94-96, 98-100 and 107 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Richards *et al.* (U.S. Patent No. 5,270,201 issued 14 December 1993). Specifically, it is alleged that because the term "satellite artificial chromosome" (SATAC) is indefinite, it is interpreted broadly to encompass "artificial chromosomes." Therefore, it is

concluded in the Office Action that Richards *et al.* anticipates the rejected claims because it allegedly teaches a method of making an artificial plant chromosome, using it to transform plant cells (wherein the plant cell is a protoplast), wherein the artificial chromosome encodes a gene product (the prior art herbicide resistant form of a normally occurring enzyme is a heterologous encoded gene product), wherein the artificial chromosome is introduced by direct DNA transfer and wherein the plant cell is from a monocot, dicot or algae.

The rejection is respectfully traversed.

ANALYSIS

The Claims

The rejected claims are directed to a method for producing a transgenic plant that includes introducing a **satellite artificial chromosome (SATAC)** into a plant cell and growing the plant cell under conditions to produce a transgenic plant. Dependent claims specify that the plant cell is a protoplast, that the SATAC contains DNA encoding a gene product, that the SATAC is introduced by direct DNA transfer, that the cell or protoplast is from a monocot, dicot or algae, and that the cell or protoplast is selected from tobacco, tomato, potato, petunia, wheat, rice, maize, rye, cotton, soybean, Brassica napus and lettuce.

Richards *et al.*

The cited art (Richards *et al.*) describes the isolation of a telomeric clone from A. thaliana and methods that may be used to obtain ARS and centromeric sequences from A. thaliana. Example 19, which is prophetic, purports to provide a method for assembling the telomeres, ARS and centromere into an artificial chromosome. No where in Richards *et al.* is a satellite artificial chromosome disclosed or is a method of making such an artificial chromosome through amplification of heterochromatin or by any other means. No where in Richards *et al.* is an artificial chromosome that is predominantly heterochromatin disclosed. As such, it is readily apparent that Richards *et al.* cannot anticipate the claimed methods of producing a transgenic plant which include a step of

introducing a satellite artificial chromosome into a plant cell. Furthermore, the readily apparent failure of Richards *et al.* to disclose a satellite artificial chromosome supports Applicant's assertion that the term "satellite artificial chromosome" is not indefinite as alleged in the Office Action.

* * *

In view of the above amendments and remarks, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
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Exhibit A

A. Revision history for X76056

GI	Version	Update Date	Status	I	II
558681	1	Oct 17 2002 5:30 AM	Live	◉	○
558681	1	Mar 9 1999 6:21 AM	Dead	○	○
558681	1	Aug 22 1997 4:32 AM	Dead	○	○
558681	1	May 31 1996 11:08 PM	Dead	○	○
558681	1	May 24 1995 5:24 PM	Dead	○	○
558681	1	Oct 21 1994 2:47 PM	Dead	○	○
511046	0	Jul 24 1994 12:18 AM	Dead	○	○
511046	0	Jul 17 1994 12:40 AM	Dead	○	◉

Accession X76056.1 was first seen at NCBI on Jul 17 1994 12:40 AM

Exhibit B

A. Revision history for D76443

GI	Version	Update Date	Status	I	II
1040699	1	Oct 6 2005 6:19 PM	Live	◉	○
1040699	1	Aug 1 2002 1:19 AM	Dead	○	◉
1040699	1	Jul 24 2002 2:52 PM	Dead	○	○
1040699	1	Mar 17 1999 10:23 PM	Dead	○	○
1040699	1	Jun 4 1997 6:45 PM	Dead	○	○
1040699	1	Mar 25 1997 12:31 AM	Dead	○	○
1040699	1	Feb 17 1997 3:17 AM	Dead	○	○
1040699	1	Oct 25 1995 2:07 AM	Dead	○	○

Accession D76443 was first seen at NCBI on Oct 25 1995 2:07 AM